

The Implications of Insurance Status on Presentation, Surgical Management and Mortality among Non-Metastatic Breast Cancer Patients in Indiana

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Abstract:

Introduction: The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) seeks to reduce healthcare disparities by providing uninsured and underinsured women access to screening mammograms. The objective of this study is to identify the differences in presentation, surgical management and mortality among non-metastatic uninsured patients diagnosed through Indiana's Breast and Cervical Cancer Program (IN-BCCP) compared to patients with private and government (Medicare or Medicaid) insurance.

Methods: Study data was obtained using the Indiana state cancer registry and IN-BCCP. Women ages 50-64 with an index diagnosis of stage 0-III breast cancer from January 1st, 2006 to December 31, 2013, were included in the study. Bivariate intergroup analysis was conducted. Kaplan Meier estimates between insurance types were compared using the log rank test. All-cause mortality was evaluated using a mixed effects model.

Results: The groups differed significantly for sociodemographic and clinical variables. Uninsured IN-BCCP patients presented with later disease stage ($p < 0.001$) and had the highest overall mortality (HR 2.2, $p = 0.003$). Surgical management only differed among stage III patients ($p = 0.012$).

Conclusion: To improve insurance-based disparities in Indiana, implementation of the BCCP in conjunction with expansion of insurance coverage to vulnerable low-income populations need to be optimized.

Introduction:

Since the implementation of the Patient Protection and Affordable Care Act (ACA), insurance and access to healthcare have been at the forefront of national discourse. For breast cancer patients, insurance status has been linked to disparities in stage of presentation, treatment and survival.¹⁻³ For women who are uninsured, underinsured or underserved, the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), managed by the Centers for Disease Control and Prevention, provides a means to undergo free screening mammography and receive subsequent treatment through state funded insurance.⁴ The Indiana Breast and Cervical Cancer Program (IN-BCCP) is the state's iteration of the NBCCEDP.

Criteria for entry into the IN-BCCP screening mammography program includes (1) age 50-64 years, (2) lack of healthcare coverage for screening mammography, and (3) income up to 200% of the federal poverty level.⁵ Patients meeting criteria for participation in the program, who ultimately are diagnosed with breast cancer, are eligible for Medicaid (MA 12) under the Indiana Breast and Cervical Cancer Treatment Act.

To date, most studies evaluating the NBCCEDP have focused on comparing presentation, treatment and clinical outcomes, such as all-cause and cancer specific mortality, between breast cancer patients diagnosed through NBCCEDP and non-NBCCEDP patients in state cancer registries⁶⁻⁸. However, few studies have evaluated NBCCEDP and non-NBCCEDP data through the lens of insurance status at diagnosis.⁸ Reviewing the data with a focus on insurance status at diagnosis improves our understanding of how access to screening by the NBCCEDP mitigates insurance-based disparities in disease presentation and clinical outcomes. To this end, the objective of this study is to understand the differences in presentation, surgical management and all-cause mortality between uninsured IN-BCCP breast cancer patients at diagnosis and privately or government insured patients in the Indiana cancer registry. We hypothesize that utilization of the IN-BCCP by uninsured low-income Hoosiers will result in

equivalent stage of presentation, surgery use and similar all-cause mortality when compared to privately insured, Medicare and Medicaid patients.

Methods:

This study is an observational cohort study of breast cancer patients identified in both the Indiana State Cancer Registry (ISCR) and IN-BCCP, maintained by the Indiana State Department of Health. The Indiana Network for Patient Care (INPC) was used to supplement data collected in the state cancer registry; the INPC is a state level database with access to the electronic medical records of multiple healthcare systems in Indiana.⁹

Population:

Women ages 50-64 (at time of diagnosis) with stage 0-III breast cancer diagnosed between January 1, 2006, and December 31, 2013, were identified in both the ISCR and IN-BCCP. The 50-64 age range encompasses the age eligibility criteria for participation in breast cancer screening through the IN-BCCP.

Measures:

The sociodemographic variables assessed included insurance type at diagnosis, area of residence (urban versus rural), age, race/ethnicity (black, white other), area poverty level (based on county census level data), and education (based on county census level data). The insurance types at diagnosis evaluated were uninsured (IN-BCCP), private, Medicaid, and Medicare. The uninsured group were those who were enrolled in the IN-BCCP.

Race/ethnicity groups designated as Asian, Native American, Pacific Islander and other were aggregated into a single “other” category due to their small numbers. The poverty level was divided into three groups based on the percentage of residents in the patient’s zip code living below the poverty level.

The groups included—low (3.9%- 14.5%), moderate (14.6%-18.3%) and high (18.4% -24.7%).

Comorbidities were classified according to the Charlson Deyo morbidity index (0, 1-2, ≥ 3).

Clinical variables of interest included pathologic stage 0-III (based on AJCC 6th edition), estrogen receptor status [ER], progesterone receptor status [PR] and human epidermal growth factor receptor 2 status [Her-2]). We excluded stage 0 patients from our tabulation of Her 2-receptor status, as this is not routinely performed in patients with ductal carcinoma in situ. Due to the small proportion of subjects with stage II breast cancer in the IN-BCCP (2% of the eligible population), stage I and II patients were combined into a single group. Surgery type was divided into breast conservation surgery (BCS), mastectomy and no surgery. BCS included partial mastectomy, lumpectomy and excisional biopsy.

Analysis

Bivariate intergroup analysis evaluating differences in sociodemographic variables, clinical variables and surgical management were conducted using chi squared, student T tests, and ANOVA, followed by Tukey's pairwise comparison of the means as appropriate. Subgroup bivariate analysis comparing differences in surgery type were stratified by stage.

Survival analysis among stage I-III breast cancer patients was conducted using Kaplan Meier estimates at 3 years and 5 years, using the outcome of all-cause mortality. Stage 0 patients were omitted due to a high survival rate in this cohort. The four insurance types at diagnosis were compared using the log rank test. A mixed-effect survival model was created to better define the relationship between all-cause mortality and insurance status at diagnosis. We used a mixed-effects parametric survival model that allowed us to control for the clustering effect at the county level, due to poverty and education level data coming from the same county. Variables in the model included insurance type, race/ethnicity, poverty group (low, moderate, high), education, area of residence, surgery type, receipt of radiation, pathologic stage, and comorbidities. The variables in the model were selected due their acceptance in the literature as variables that affect mortality among breast cancer patients.^{6,7,10} All statistical analyses were

performed in Stata software version 14.2.

Results:

Study Population Description

The study population included 1462 patients from ages 50-64 years with stage 0-III breast cancer diagnosed from 01/01/2006 through 12/31/2013. The distribution of insurance at diagnosis included: IN-BCCP 350 (23.9%), private insurance 786 (53.8%), Medicaid 162 (11.1%), and Medicare 164 (11.2%). The majority of patients in the study were white 1196 (81.8%), with no comorbidities 1317 (90%), had obtained a high school diploma 86.5%, and resided in an urban area 1139 (78%). The population was evenly distributed among the three poverty groups of low 491 (33.6%), moderate 496 (34%) and high 474 (32.44%) (Table 1).

Disease Presentation and Surgical Management between Insurance Groups

The insurance groups differed on stage at presentation ($p < 0.001$). Specifically, a higher percentage of IN-BCCP patients presented with stage III disease compared to Medicare, Medicaid and private insurance. There was a significant difference between insurance groups on hormone receptor status ER ($P < 0.001$), PR ($P < 0.001$), and Her-2 status ($P < 0.001$), with IN-BCCP presenting with highest incidence of Her-2 positive disease (Table 2).

Bivariate analysis showed a significant difference between the groups on surgery type (BCS vs Mastectomy) (Table 3). However, when the data was stratified by stage, the difference in surgery type only persisted among stage III patients ($p = 0.012$) (not shown).

Subset analysis conducted among BCS patients to evaluate radiation therapy use showed no difference between the insurance groups on receipt of radiation therapy after BCS ($p = 0.873$) (Table 3).

All-cause Mortality Differences by Insurance Group

On Kaplan-Meier analysis, IN-BCCP patients had the worst all-cause mortality ($p = 0.000$) (Figure 1). The divergence of all-cause mortality among the IN-BCCP from the other insurance types started at 3-years ($p = 0.0241$) (Figure 2) and continued at 5-years ($p = 0.0204$) (Figure 3).

On multivariable analysis, the difference in all-cause mortality between patients within the IN-BCCP and those with private or government insurance persisted, as shown in Table 4. With private insurance as the reference group, patients in the IN-BCCP had the highest all-cause mortality [HR 2.2, (95% CI 1.3, 2.6), $p = 0.003$] compared to those with Medicaid [HR 1.4, (95% CI 0.9, 2.02), $p = 0.216$] and Medicare [1.4 (95% CI 0.8, 2.6), $p = 0.257$]. Lack of surgery [HR 2.9, (95% CI 1.5, 5.9), $p = 0.001$] and presence of multiple comorbidities [HR 2.6, (95% CI 1.4, 4.5), ($p = 0.001$)] were also associated with an increased all-cause mortality.

Discussion

This study is the first to evaluate the differences in presentation, surgical management, and mortality among uninsured non-metastatic breast cancer patients diagnosed through the IN-BCCP, compared to those with private or government insurance. NBCCEDP programs, such as the IN-BCCP are designed to reduce healthcare disparities by increasing access to breast and cervical cancer screening among underserved women.⁴ For breast cancer patients, access to screening mammography is vital for early detection and improved survival.¹¹ While these programs receive a combination of federal and state funding, they are exclusively administered by state governments. Therefore, evaluation of the success of these individual programs at the state level is important to understand how different local contexts affect the impact of the program. In addition, knowledge of the influence of insurance status at diagnosis on clinical outcomes may inform future state policy and health insurance resource allocation.

Our finding of uninsured IN-BCCP patients presenting with a more advanced cancer stage is consistent with other studies evaluating insurance-based disparities and stage of presentation among breast cancer patients.^{2,12,13} In their examination of breast cancer patients in the National Cancer

Database, Halpern et al demonstrated that uninsured patients or patients with Medicaid were more likely to present with stage II-IV disease than stage I, when compared to their privately-insured counterparts.¹⁴ Hsu et al. confirmed this finding with their evaluation of the Surveillance Epidemiology End Result database, noting patients with Medicaid and the uninsured presented with a later stage disease compared to the privately insured¹⁵. Possible explanations for later disease presentation among the uninsured or Medicaid patients are lack of access to screening or infrequent use of screening services.¹⁴ However, since our uninsured population participated in a program intended to increase screening access, the disparity in stage may reflect patients using the program when symptomatic, or alternatively, being more likely to develop aggressive types of breast cancer that develop within established screening intervals.

There is heterogeneity in the literature regarding the association between insurance and surgical treatment. Yet in general, patients with private insurance have higher rates of BCS than their government (Medicare, Medicaid) insured or uninsured counterparts.^{1,12,16,17} In our study, bivariate analysis showed significant differences in surgery type between the insurance groups. Nevertheless, when stratified by stage, only stage III breast cancer patients differed significantly on surgery type. Specifically, stage III IN-BCCP patients were the least likely to undergo mastectomy compared to private, Medicaid and Medicare insurance (not shown). This result prompted further analysis evaluating the use of radiation therapy among all patients who underwent BCS. The analysis revealed no difference between the insurance groups in the use of radiation therapy thus indicating insurance type did not appear to affect receipt of the standard of care of BCS plus radiation therapy. This is meaningful as studies have shown a combination of BCS and radiation therapy improve disease specific survival.¹⁸ The eligibility for Indiana Medicaid (MA-12) for BCCP patients was enacted in 2009. Since this study covers the period between 2006 through 2013, a segment of the population was affected by the 2009 Medicaid expansion to the BCCP population. Thus, it is possible that patients who were enrolled in Medicaid gained increased access to radiation therapy, thus explaining the lack of a significant difference in the use of radiation therapy among patients undergoing BCS across insurance types. Future studies of Medicaid expansion in

Indiana should evaluate differences in outcomes before and after expansion of Medicaid among breast cancer patients.

Multiple studies have confirmed early detection through screening mammography improves mortality among breast cancer patients.¹¹ As stated previously, state programs supported by the NBCCEDP aim to improve access in the hopes of improved outcomes. In our unadjusted Kaplan-Meier analysis we noted a divergence in all-cause mortality between the insurance types starting at 3 years from diagnosis. IN-BCCP patients had worse mortality than private, Medicare or Medicaid patients at 3 years from diagnosis. This difference in all-cause mortality was confirmed in multivariate analysis (HR 2.2). The association between worsening all-cause mortality and lack of insurance is consistent with other studies evaluating insurance-based healthcare disparities.^{13,19} However, our state-based finding of no difference in all-cause mortality between Medicaid and privately insured breast cancer patients indicates that having some type of insurance at diagnosis may diminish disparities in clinical outcomes.

One potential explanation for the disparities in survival between insurance types could be the possibility of more symptomatic breast cancer (i.e. presenting with a palpable mass) among the BCCP patients. Studies indicate cancers discovered on screening mammography are smaller and less likely to be node positive, subsequently resulting in a shift to earlier stages at presentation, in conjunction with more favorable overall and breast cancer specific survival.²⁰⁻²² Therefore, if we speculate that more BCCP patients, compared to other insurance types, are receiving diagnostic mammography as their index imaging modality, one could argue they are less likely to benefit from mammography. Nonetheless, the benefits of screening mammography may be overestimated due to length time bias and lead time bias.^{23,24} Furthermore, the absolute benefit of screening is small with a Cochrane review showing 1 death avoided for every 2000 women screened.²⁵ For this study, we believe the difference in all-cause mortality between the IN-BCCP and their insured counterparts is most likely multifactorial and may include an interplay among greater unmet medical needs, socioeconomic stress, and delays in pursuing treatment once diagnosed.^{10,26-28} Future studies should consider tracking how long patients have been screened in

different breast cancer screening programs, or insurance programs for that matter, to better understand whether any cancers diagnosed were based upon first-time or interval screenings, which may be associated with different prognoses.

Limitations

We anticipate the level of awareness--and subsequent referrals--to the IN-BCCP by patients, healthcare providers and health systems may be the driving force behind patient enrollment in the BCCP. As a result, these varying levels of awareness may result in a selection bias in this cohort. Another limitation of the study dataset is our inability to verify the use of chemotherapy and hormone therapy in the study population. Both modalities have been shown to improve survival in breast cancer patients so full adjustment for these factors could affect our results.

The cancer registry also does not ascertain if patients' breast abnormality were detected on physical exam by the patient or physician. Furthermore, the registry does not clarify if the first imaging modality was screening or diagnostic mammography. This information would have been useful in understanding if the differences in stage of presentation and survival were due to difference in presentation (symptomatic vs asymptomatic).

The study evaluated all-cause mortality because breast cancer specific mortality was not available for the dataset. As a result, differences in breast cancer specific mortality may still be present. In addition, the absolute benefits of mammography are very small, and our sample may not be adequately powered to reflect that benefit. Nonetheless, because all-cause mortality is not affected by bias in classifying the cause of death, it is an important outcome to measure in cancer screening programs.²⁹ Finally, the interpretation of differences in hormone receptor status should be made with caution due the high level of missingness, approximately 50%, due to changes in the data elements routinely collected by the cancer registry over time.

Conclusion

Low-income individuals are among the most sensitive to changes in insurance policy due to significant insurance-based disparities in healthcare access and clinical outcomes. This study helps to better understand the impact of a federally-funded, state-administered cancer screening program upon insurance-based disparities and whether participation in the program mitigates prior lack of insurance. Based on the data presented here, breast cancer patients in Indiana utilizing the BCCP program have a worse all-cause mortality and are more likely to present with a later stage of breast cancer than patients with private or government insurance. Our findings indicate that outcomes for breast cancer patients with Medicaid at diagnosis differ from those with IN-BCCP, suggesting that further expansion of health insurance in the state may lead to earlier detection and improved survival.

Additional consideration may also be directed towards promotion and implementation of programs such as the IN-BCCP to insure the timely receipt of screening, or perhaps expand services beyond screening alone. Current estimates from the Indiana State Department of Health (ISDH) indicate that in 2014 over one quarter of Hoosier women were eligible for cervical or breast screening through the IN-BCCP. From 2011-2017, 4,275 women underwent clinical breast exam, mammography or ultrasound evaluation using BCCP resources. Of these, 2,800 women underwent screening mammography through the program.³⁰ Therefore, only a very small fraction of those eligible for the IN-BCCP participated in the program. Without universal insurance, IN-BCCP clearly remains a necessary option of last resort to enable access to community-based breast cancer screening.

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Figure 3: All-cause Mortality at 5 years between IN-BCCP and Other Insurance Types

Table 4: Multivariable Mixed Effect Model evaluating All-cause Mortality

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Table 1: Study Population Sociodemographic Variables by Insurance Status at Diagnosis*

Variables	Total Sample	IN-BCCP	Medicaid	Medicare	Private Insurance	P-value
Total Patients	1462	350	162	164	786	
Age						
Mean (years)	57.3	56.8	57.1	57.1	57.1	<0.001
Median (years)	57.2	56.6	57	57	57	
Comorbidities						<0.001
0	1317 (90)	315 (90)	140 (86.4)	129 (78.7)	733(93.3)	
1-2	138 (9.4)	33 (9.4)	21 (13)	31 (19)	53 (6.7)	
≥3	7 (0.5)	2 (0.6)	1 (0.6)	4 (2.4)	0	
Race						<0.001
White	1196 (81.8)	297 (84.9)	108 (66.7)	106 (64.6)	685 (87.1)	
Black	252 (17.2)	47 (13.4)	53 (32.7)	58 (35.4)	94 (12)	
Other	14 (1)	6 (1.71)	1 (0.6)	0	7 (0.9)	
Poverty Status						<0.001
Low	491 (33.6)	181 (51.7)	22 (13.6)	24 (14.6)	264 (33.6)	
Moderate	196 (34)	109 (31.1)	68 (42)	65 (39.6)	254 (32.4)	
High	474 (32.4)	60 (17.4)	72 (44.4)	75 (45.7)	267 (34)	
Metro Status†						<0.001
Rural	286 (19.6)	80 (22.9)	20 (12.4)	21 (12.8)	165 (21)	
Urban	1139 (78)	270 (77.1)	141 (87)	141 (86)	587 (74.7)	
unknown	37 (2.5)	0	1 (0.62)	2 (1.1)	34 (4.3)	
Education‡						<0.001
High School (SD)	86.5% (3.4)	86.9% (3.4)	85% (1.8)	85.8% (2.4)	86.9% (3.7)	
College (SD)	23.7% (8.9)	21.4% (7.3)	24.1 % (6.1)	24.6% (6.6)	24.6% (10.2)	<0.001
Follow-Up Time						0.0002
Mean (days)	501.8	489.5	647	611.2	489.5	
Median (days)	272	211.5	505.5	386	211.5	

*Data points reported as N (%) unless specified otherwise. Data may not add up to 100% due to rounding.

†Metropolitan status

‡Education level describes the percent of the population that graduated from high school or college. This information was based on county level census data.

Table 2: Study Clinical Variables by Insurance at Diagnosis*

Variable	Total Sample (n=1462)	IN-BCCP (n=350)	Medicaid (n=162)	Medicare (n=164)	Private Insurance (n=786)	P-value
Stage						
0	249 (17.3)	46(13.6)	13 (8.3)	28 (17.5)	162 (20.6)	<0.001
I -II	948 (65.8)	202 (59.6)	111 (71.2)	100 (62.5)	535 (68.2)	
III	242 (16.8)	91 (26.8)	32 (20.5)	32 (20)	87 (11.1)	
Estrogen						<0.001
No	241 (16.5)	59 (14.9)	28 (10.5)	37 (15.9)	117 (10.6)	
Yes	793 (54.2)	138 (41.4)	114 (77.2)	91 (62.2)	450 (61.9)	
Unknown	428 (29.3)	153 (43.7)	20 (12.4)	36 (22)	219 (27.9)	
Progesterone						<0.001
No	360 (24.6)	74 (22.6)	50 (30.9)	50 (30.5)	186 (24.1)	
Yes	656 (44.9)	119 (32.6)	91 (56.2)	74 (45.1)	372 (47)	
Unknown	446 (30.5)	157 (44.9)	21 (13)	40 (24.4)	228 (29)	
Her 2†						<0.001
No	634 (51.8)	97 (31.9)	104 (69.8)	82 (60.3)	343 (55)	
Yes	177 (14.5)	51 (16.8)	23 (15.4)	19 (14)	83 (13.3)	
Unknown	413 (33.7)	156 (51.3)	22 (14.8)	35 (25.7)	198 (31.7)	

*Data points reported as N (%) unless specified otherwise. Total sample size for each variable may not add up to 1462 due to missing data. Data may not add up to 100% due to rounding.

† This variable excludes patients with Ductal Carcinoma In-Situ.

Table 3: Comparison of Surgical Management and Radiation among Insurance Types*

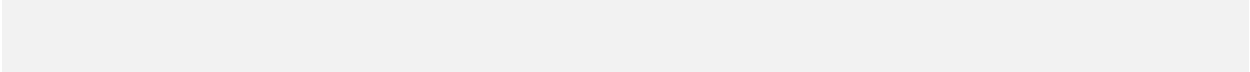
Characteristic	Total Sample (n=1462)	IN-BCCP (n=350)	Medicaid (n=162)	Medicare (n=164)	Private Insurance (n=786)	P Value
Surgery						0.004
None	83 (5.7)	24 (6.9)	11 (6.8)	18 (11)	30 (3.8)	
BCS	706 (48.3)	172 (49.1)	64 (39.5)	73 (44.5)	397 (50.6)	
Mastectomy	672 (46)	154 (44)	87 (53.7)	73 (44.5)	358 (45.6)	
Radiation therapy						0.738
No	961 (65.9)	221 (63.1)	106 (65.8)	108 (66.3)	526 (67)	
Yes	498 (34.1)	129 (36.9)	55(34.2)	55 (33.7)	259 (33)	
BCS only†	351 (49.8)	83(48.3)	32(50)	34 (46.6)	202 (51)	0.873
BCS + Radiation	354 (50.2)	89 (51.7)	32(50)	39 (53.4)	194 (49)	

* Data points reported as N (%) unless specified otherwise. Data may not add up to 100% due to rounding.

†This row only evaluated patients who underwent BCS. One patient excluded due to missing data.

Table 4: Multivariable Mixed Effect Model evaluating All-cause Mortality

Variables	Hazard Ratio [95% CI]	p-value
<u>Insurance</u>		
Private	REF	
No insurance (IN-BCCP)	2.2 (1.3, 3.6)	0.003
Medicaid	1.4 (0.9, 2.2)	0.216
Medicare	1.4 (0.8, 2.6)	0.257
<u>Race</u>		
White	REF	
Black	1 (0.7, 1.5)	0.993
<u>Poverty Level</u>		
Low	REF	
Medium	1.0 (0.5, 1.8)	0.865
High	1.4 (0.7, 2.9)	0.345
<u>Education*</u>		
High school Diploma	1.0 (0.9, 1.1)	0.588
College Degree	1.0 (0.9, 1.0)	0.875
<u>Metropolitan Status</u>		
Rural	REF	
Urban	0.8 (0.5, 1.5)	0.482
Unknown	0.3 (0, 3.0)	0.313
<u>Surgery</u>		
BCS	REF	
Mastectomy	1.0 (0.7, 1.6)	0.878
No Surgery	2.9 (1.5, 5.9)	0.002
<u>Radiation therapy</u>		
No	REF	
Yes	0.7 (0.4, 1.2)	0.188
<u>Stage</u>		
Stage III	REF	
Stage I and II	0.4 (0.3, 0.6)	0.001
<u>Comorbidities</u>		
0	REF	
1-2	2.1 (1.0, 4.5)	0.053
≥3	2.6 (1.5, 4.5)	0.001



*Educational attainment compared percent of county residents that had completed college or high school to counties that had 1% lower county level education attainment. This information was retrieved from census level data.